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1. AGENCY USE ONLY (Leave blank) 2. REPORT DATE 3. REPORT TYPE AND DATES COVERED
Technical Report #

4. TITLE AND SUBTITLE Photogenerated Amines in Polymer Curing and Imaging: Design and Synthesis of [(3',5'-Dimethoxybenzoinyl)oxy]carbonyl Carbamates as Novel Photoprecursors of Amines. 5. FUNDING NUMBERS
C N00014-91-1338

6. AUTHOR(S)
Jean M.J. Fréchet, James F. Cameron, and C. Grant Willson

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Cornell University
Dept. of Chemistry, Baker Laboratory
Ithaca, New York 14853-1301 8. PERFORMING ORGANIZATION
REPORT NUMBER
C N00014-91-1338

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Department of the Navy
Office of Naval Research
800 North Quincy Street
Arlington, VA 22217-5000 10. SPONSORING/MONITORING
AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
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13. ABSTRACT (Maximum 200 words)
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19950123 005

14. SUBJECT TERMS Photopolymer, curing, imaging, photogenerated base microlithography, display technology, amine precursor photogenerated catalyst, photochemistry 15. NUMBER OF PAGES
12 16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT
Unclassified 18. SECURITY CLASSIFICATION OF THIS PAGE
Unclassified 19. SECURITY CLASSIFICATION OF ABSTRACT
Unclassified 20. LIMITATION OF ABSTRACT
UL

OFFICE OF NAVAL RESEARCH

Grant # N00014-91-J-1338

R&T Code 313t003--06

Dr. Kenneth J. Wynne

Technical Report #20

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By Jean M.J. Fréchet, James F. Cameron, and C. Grant Willson

Department of Chemistry, Baker Laboratory
Cornell University, Ithaca, New York 14853-1301

January 20, 1995

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**Photogenerated Amines in Polymer Curing and Imaging: Design
and Synthesis of [(3',5'-Dimethoxybenzoinyl)oxy]carbonyl
Carbamates as Novel Photoprecursors of Amines.**

Jean M.J. Fréchet^a, James F. Cameron^b, and C. Grant Willson^b

(a) Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, NY 14853-1301

(b) IBM Research Division, Almaden Research Center, 650 Harry Road, San Jose, CA 95120.

ABSTRACT:

The design of novel compounds that can be used to photogenerate amines when subjected to UV irradiation is explored. These novel compounds are [(3',5'-dimethoxybenzoinyl)oxy]carbonyl carbamates that undergo a light induced photocyclization with release of a free primary or secondary amine. The novel photogenerators can be used with 250-350 nm light in a process that is essentially free of side-reactions. These carbamate photogenerators of base may be useful both in polymer curing and imaging processes, and as protecting groups in organic synthesis.

Recently, we developed a strategy for base photogeneration by masking amines and diamines as photoactive carbamates¹. Under the action of light, these neutral carbamates decompose to liberate the free base. However, we found the commonly used photolabile amino protecting groups, e.g., the 3,5-dimethoxy- α,α -dimethylbenzyloxycarbonyl and *o*-nitrobenzyloxycarbonyl moieties, undergo somewhat complex photochemistry which may also be complicated by deleterious side reactions upon prolonged photolysis. In order to expand the current applicability of photogenerated amines we have investigated new photochemistry that would allow for efficient unmasking of amino groups. With this goal in mind, we focused on the rich photochemistry offered by the desyl chromophore. While the parent desyl chromophore is well known to undergo photocleavage via classical photochemical pathways such as α -cleavage (Norrish Type I), meta methoxy substitution causes photocyclization to become the major photocleavage pathway. For instance, Sheehan *et. al.*² reported photolysis of 3',5'-dimethoxybenzoin acetate affords 5,7-dimethoxy-2-phenylbenzo[b]furan as the major product. In this case, photocyclization is accompanied by formation of acetic acid. This unique photoreactivity has led to the use of methoxy substituted benzoin esters as photolabile carboxyl protecting groups^{2,3}. More recently, the photocyclization of substituted benzoin esters has been applied to the caged release of phosphate derivatives⁴⁻⁷.

Based on the unique mode of photochemistry offered by 3',5'-dimethoxybenzoin esters, we investigated the 3',5'-dimethoxybenzoin chromophore as a novel photolabile amino protecting group. We now report

preliminary results on the photoliberation of amines from 3',5'-dimethoxybenzoin carbamates according to Scheme 1.

3',5'-Dimethoxybenzoin cyclohexyl carbamate (**1**) was prepared by reaction of cyclohexyl isocyanate with the corresponding benzoin in refluxing benzene. Piperidinyl carbamate (**2**) was prepared by reaction of piperidine with the p-nitrophenyl mixed carbonate of 3',5'-dimethoxybenzoin. Preparative photolysis of 3',5'-dimethoxybenzoin cyclohexyl carbamate (**1**), 5mM in acetonitrile solution, proceeded smoothly upon irradiation in a Rayonet photochemical reactor with 350nm lamps for 2h. The major products were cyclohexylamine and 5,7-dimethoxy-2-phenylbenzo[b]furan (**1a**). The fluorescent benzo[b]furan (**1a**) was isolated in excellent yield (80-85%) after flash chromatography and recrystallization. In our hands, the photoefficiency of the amine deblocking appears significantly greater than other commonly used photolabile amino protecting groups.

The photochemical removal of the [(3',5'-dimethoxybenzoinyl)oxy] protecting group was readily monitored by ^1H nmr spectroscopy by irradiating a 20mM solution of carbamate (**1**) in acetonitrile- d_3 . The integral of the carbamate cyclohexyl methine [CH, m, δ 3.40] decreased, while the expected multiplet of the cyclohexyl methine of free cyclohexylamine appeared at δ 2.52 and grew upon increased exposure at 350 nm in a Rayonet photochemical reactor. After 60 min., conversion to free cyclohexylamine reached 93%. In addition to cyclohexylamine, 5,7-dimethoxy-2-phenylbenzo[b]furan (**1a**) was identified as

the major by-product by ^1H nmr spectroscopy. A singlet, characteristic of the 3-benzo[b]furan proton in (1a), appears at δ 7.12 and increases in intensity with photolysis time. By comparison, photolysis of the parent benzoin cyclohexyl carbamate gives a complex photolysate in which benzo[b]furan cannot be identified¹¹. This illustrates the important role the 3',5'-dimethoxy substituents play in redirecting the mechanism of photocleavage.

Gas chromatography confirms the clean photoliberation of free cyclohexylamine and piperidine from 3',5'-dimethoxybenzoin carbamates, (1) and (2), respectively. In each case, GC-MS indicated the appropriate molecular ion for the corresponding unmasked amine. For the photolysis of cyclohexyl carbamate, (1), GC-MS indicated the major by-product was the expected 5,7-dimethoxy-2-phenylbenzo[b]furan (1a). Other minor products, present in only trace amounts, were identified as the benzylic ketone (1b), the substituted benzil (1c), N-benzoylcyclohexylamine and dicyclohexylurea (Scheme 1). Formation of these minor photoproducts can be rationalized in terms of known benzoin photochemistry. For example, the loss of the α -carbamoyloxy moiety to give benzylic ketone (1b) is consistent with the cleavage mechanism of the photolabile phenacyl protecting group⁸.

Further evidence for the photochemical rearrangement of these benzoin carbamates was obtained by following the changes in the infra-red spectrum of a

¹¹ Despite the inefficient photocyclization, a 75% conversion to free cyclohexylamine was observed. In this case, the photoliberation of amine likely proceeds via classical desyl photochemistry.

solution of benzoin carbamate (1) in dry acetonitrile with increasing UV exposure dose (Figure 1). Exposure to 350 nm radiation in a Rayonet reactor caused the gradual disappearance of both the keto carbonyl stretch (1700 cm^{-1}) and the carbamate carbonyl stretch (1723 cm^{-1}). This change is consistent with the proposed mode of photodeblocking (Scheme 1) because photocyclization liberates the free amine leading to the observed loss of both carbonyl bands. Additional evidence for the photoremoval of the protecting group was gained by monitoring the changes in the N-H stretching frequency. In this case, UV exposure at 350 nm resulted in the gradual depletion of the carbamate N-H stretch at 3360 cm^{-1} , with concomitant appearance of bands due to the photoliberated cyclohexylamine in the region 3500 to 3700 cm^{-1} . These findings are consistent with the smooth photocyclization that accompanies amine liberation during photolysis of 3',5'-dimethoxybenzoin carbamate (1).

The changes in the UV spectrum of a dilute acetonitrile solution of piperidinyl carbamate (2) with increasing photolysis time are shown in Figure 2. Two isobestic points are observed at 231 and 260 nm respectively. During irradiation of carbamate (2), the maximum originally at 243 nm is replaced by an intense absorption maximum at 300 nm, resulting from photocyclization to the conjugated benzo[b]furan (1a). This spectral change is accompanied by bleaching of the deep UV absorption in the 230-260 nm region. Overall, the change in the UV spectrum is representative of this class of benzoin carbamate and is consistent with photocyclization to form 5,7-dimethoxy-2-phenylbenzo[b]furan (1a) (Scheme 1).

A mechanism for amine liberation via the photochemical rearrangement of 3,5-dimethoxybenzoin carbamates is shown in Scheme 1. On irradiation, $n-\pi^*$ excitation of the carbonyl group leads to formation of the excited triplet state (3). Subsequent homolysis produces a radical pair (4) which undergoes rapid electron transfer to yield an ion pair (5). After ring closure, the liberated anion acts as a base. This base removes the bridgehead proton from (6), forming the benzo[b]furan photoproduct (7). The unstable carboxylated amine then loses carbon dioxide, liberating the free amine. The key step, formation of benzylic carbocation (5), is favored by substituents that can stabilize the developing positive charge. Zimmerman⁹ has shown that meta methoxy groups are particularly efficient in this regard. Since the photocyclization pathway is the preferred mode of photocleavage for 3',5'-dimethoxybenzoinyl carbamates, it seems probable that photocyclization proceeds via a meta benzylic carbocation, as in (5). Therefore, the pathway for amine generation via photocyclization is consistent with the electronic effects of meta methoxy substitution.

In conclusion, we have demonstrated the potential utility of the [(3',5'-dimethoxybenzoinyl)oxy]carbonyl moiety as a novel photolabile protecting group for primary and secondary amines. Photochemical removal of the 3',5'-dimethoxybenzoin chromophore is particularly clean, with minimal side products. This is in contrast to the photochemistry of many other photosensitive protecting groups.

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Scheme 1

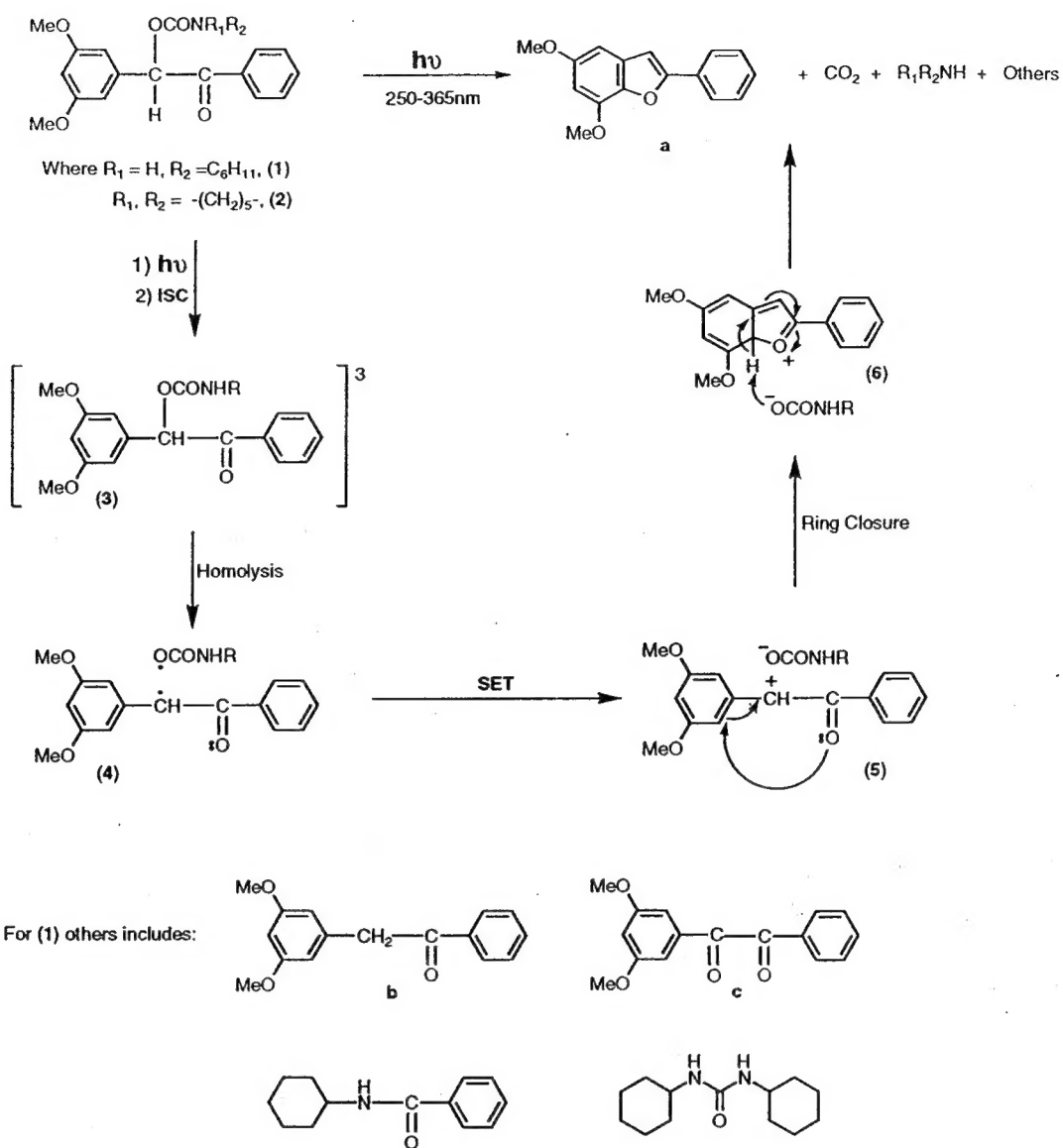


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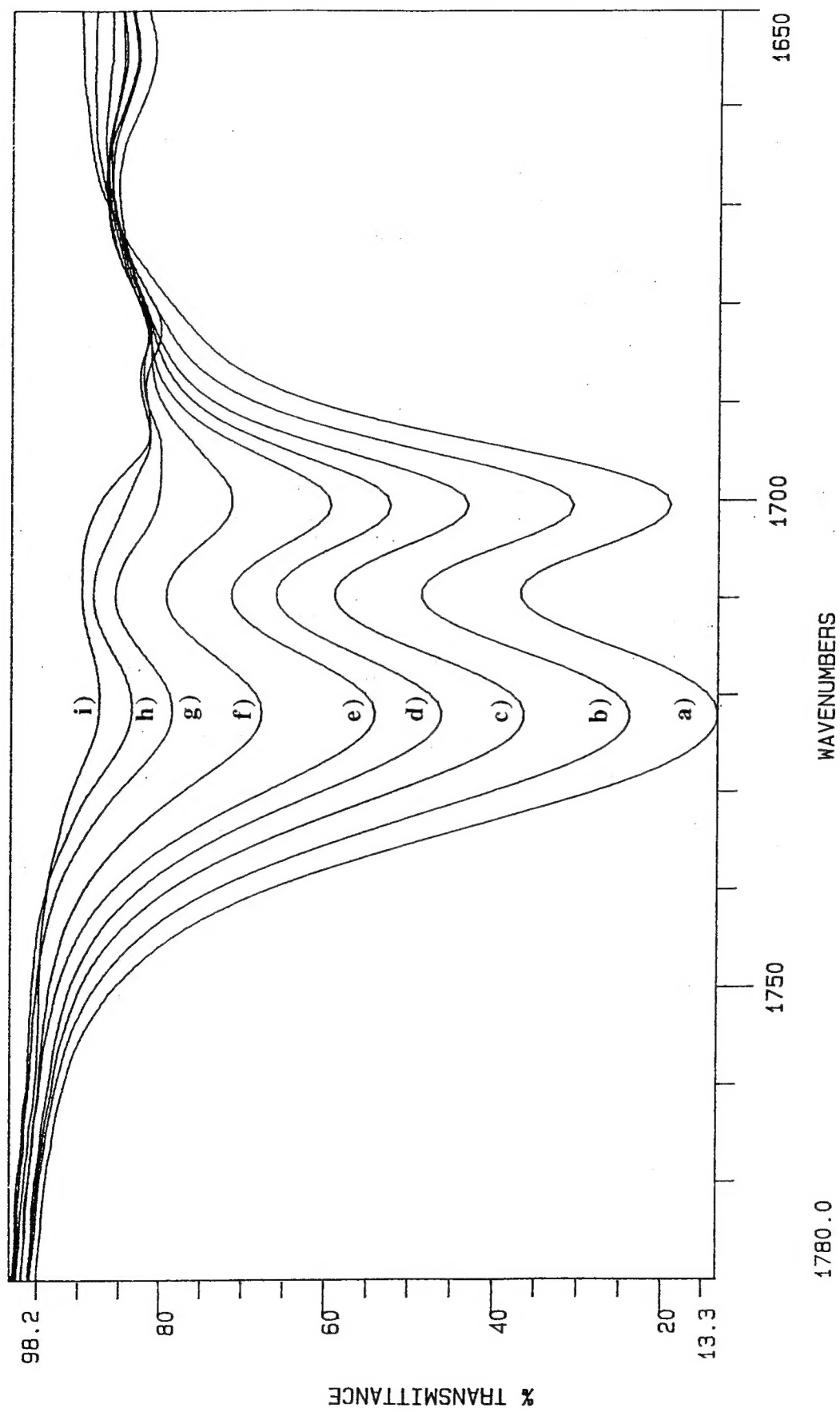
Figure 1: Change in carbonyl region of carbamate (1) as a 11.8 mM solution in MeCN with increasing 350 nm photolysis in Rayonet.

- a) Prior to exposure.
- b) After 5min exposure.
- c) After 10min exposure.
- d) After 15min exposure.
- e) After 20min exposure.
- f) After 30min exposure.
- g) After 45min exposure.
- h) After 60min exposure.
- i) After 120min exposure.

Figure 2: Change in UV spectrum of carbamate (2) as a 7.071×10^{-5} M solution in MeCN with increasing 350 nm photolysis.

- a) Prior to exposure.
- b) After 20s exposure.
- c) After 40s exposure.
- d) After 80s exposure.
- e) After 120s exposure.
- f) After 180s exposure.
- g) After 260s exposure.
- h) After 420s exposure.
- i) After 600s exposure.

Figure 1



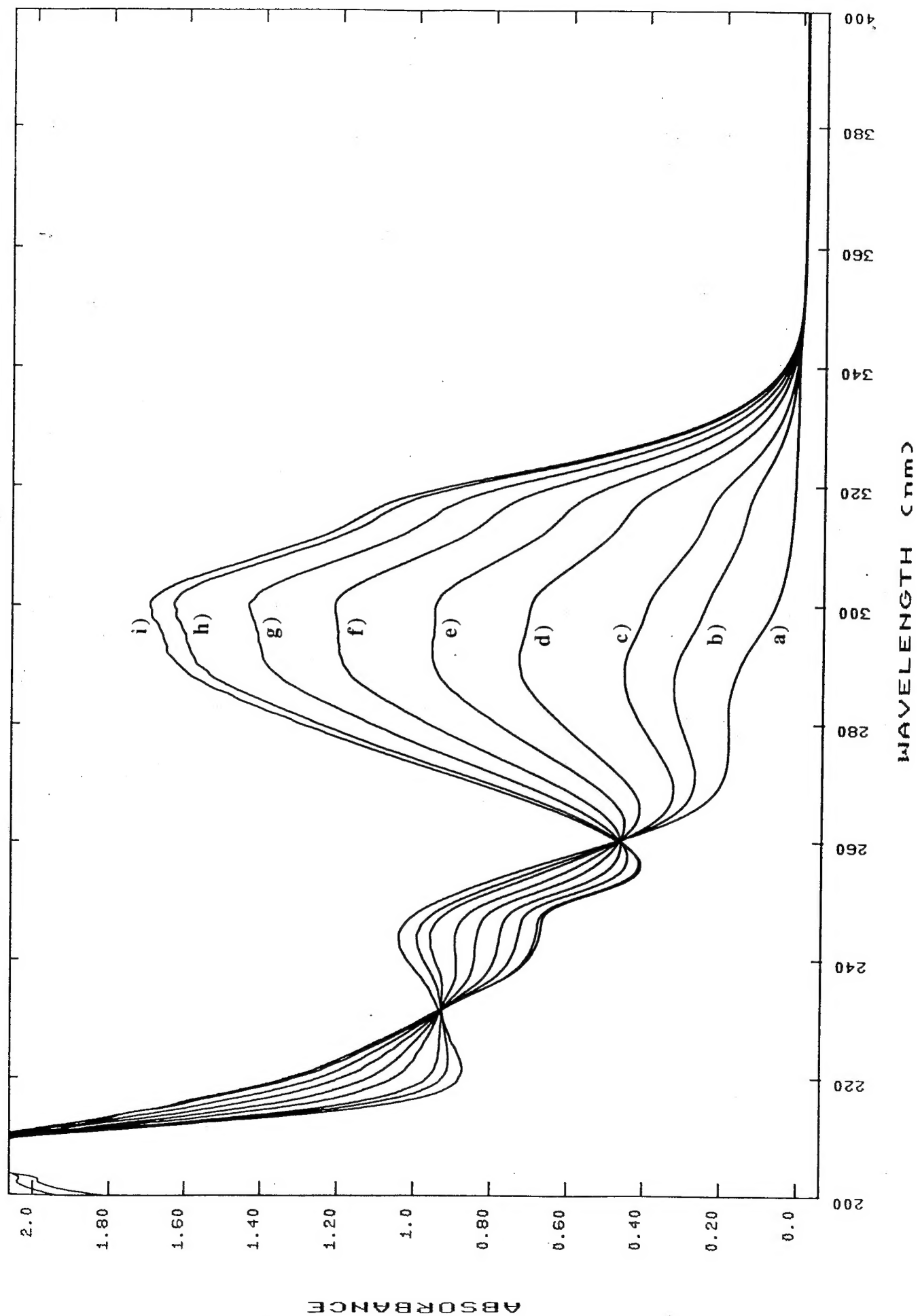


Figure 2